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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/726,024	12/02/2003	Manesh Dixit	141-239A	2662

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EXAMINER	
CLAYTOR, DEIRDRE RENEE	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
11/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/726,024	DIXIT ET AL.	
	Examiner	Art Unit	
	Renee Claytor	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6-13,16-22,24-26,28 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-4, 6-13, 16-22, 24-26, 28-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 9/18/2007 is hereby acknowledged. Claims 1, 3, 4, 6-13, 16-22, 24-26, 28 and 29 are pending.

Response to Arguments

Applicant's arguments over the 35 USC 103 rejection over Mehta (US Patent 5,837,284) in view of Mulye (US Patent 6,475,493) and Beiman (US Patent 6,312,728) have been considered and are not found persuasive. Applicants argue that the combination of references does not render the present invention obvious. More specifically, Applicants argue that Mehta does not prepare a methylphenidate tablet that employs a hydrogel polymer in the core to control the release of methylphenidate. In contrast, Mehta teaches a preparation of the invention in which a 10 percent solution of hydroxypropyl methylcellulose (HPMC) was mixed in with a solution of methylphenidate of which was then coated with a sealant. According to this teaching, it is obvious that a core is being taught that includes a hydrogel polymer because it is taught that the pellet is initially formed with the methylphenidate in combination with the hydrogel polymer together. Furthermore, because the hydrogel polymer is taught with the methylphenidate in the core, it would obviously perform the same function of controlling the release of the drug regardless of how Mehta defines HPMC.

It is further argued that Mulye fails to disclose or suggest mixing a hydrogel polymer with methylphenidate to prepare a controlled release tablet that is coated with an enteric coating containing 45% or more enteric material and processing aids. In response to this argument, the Mulye reference was used to teach that an enteric

coating in a controlled release formulation. Mulye teaches that methylphenidate is a drug that is useful in the invention and though the reference was not concentrating on the teaching of the core, it is pointed out that Mulye teaches a drug suspension with the active drug as well as HPMC. Therefore, Mulye does teach a core with a hydrogel polymer. In addition, the Mulye reference was used for the teaching of an enteric coating in controlled release formulations to aid in release of the drug.

Applicants further argue that Beiman fails to mention or suggest that methylphenidate can be used as a possible drug in the coated pellet cores. Beimen was not used to teach the active drug, but was used to teach the enteric polymers are capable of being applied to controlled release formulations at higher percentage weights than those taught by Mulye.

Accordingly, the combination of references renders the present invention obvious because a core is taught that includes a mixture of methylphenidate and a hydrogel polymer (HPMC; taught by Mehta and Mulye), an enteric coating is taught that is a mixture of 45% or more of enteric polymer and at least one convention processing aid are taught (Mulye and Beiman) and an immediate release layer of methylphenidate is taught (Mehta).

Applicant's amendments have necessitated the following modified grounds of rejection.

Claim Rejections – 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-4, 6-13, 16-22, 24-26 and 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mehta et al. (U.S. Patent 5,837,284) in view of Mulye (U.S. Patent 6,475,493) and Beiman et al. (U.S. Patent 6,312,728).

Mehta et al. teach an improved dosing of methylphenidate hydrochloride whereby two time-separated doses are provided via a single dosage unit, in which a first group of particles provides an immediate dose of methylphenidate in an amount from about 2% to about 99% by weight and a second group of particles provides a second dose of methylphenidate in an amount from about 2% to about 75% with a binder (meeting the limitations of claims 1, 21-22; Col. 1, lines 13-17 and Col. 3, lines 41-43). Mehta et al. further teach a coating that delays the release of the methylphenidate (Col. 4, lines 32-36). The dosage unit is comprised of hydroxypropyl methylcellulose (meeting the limitations of claims 6-7 and 16; Col. 10, lines 42-50). Mehta et al. further teach that the maximum concentration of the first dose occurs from about 1 hour to about 3 hours after ingestion, which is followed by a period when no drug is released which lasts approximately 2-6 hours, and the second dose is released about 6 hours following administration (meeting the limitations of claims 17, 28-29; Col. 5, lines 37-51 and Fig. 2).

Mehta et al. does not teach a diluent in the core, processing aids (enumerated in claims 8-9), that the coating is specifically made up of enteric coating polymers, peak blood plasma levels in the immediate release and extended release portions, a maximum plasma concentration up to about 20 ng/ml, and AUC $_{0-24}$ up to about 200 ng/ml.

Mulye teaches a coating composition in a controlled release pharmaceutical composition which comprises an enteric polymer (Col. 4, lines 59-62). Active medications that can be used in the composition include methylphenidate (Col. 9, line 42). The compositions contain lactose (meeting the limitations of claims 3-4; Col. 11, line 41) as well as colloidal silicon dioxide and magnesium stearate (meeting the limitations of claims 8 and 9; Col.8, lines 4-5). Enteric polymers are present, including methacrylic acid copolymer (meeting the limitations of claims 1, 10-11; Col. 6, lines 28-29) and zein (further meeting the limitation of claim 11; Col. 12, line 22).

Similar to the teachings of Mehta et al. and Mulye, Beimen et al. teach oral dosage delivery systems comprised of a core comprising a therapeutic agent, an enteric polymer coating over said core, a coating of said therapeutic agent over enteric polymer coat and a protective coating (Col. 7, lines 5-19). Beimen et al. teach that the enteric polymer coating may also contain processing aids, similar to the coating of present claims 1, 21 and 22 (Col. 8, lines 8-10). The most preferred enteric coating is Eudragit L30D-55, which is a methacrylic acid copolymer, and is applied as a 45-55 % weight aqueous solution (meeting the limitation of claims 21-22; Col. 9, lines 11-18).

Furthermore, it is obvious to vary and/or optimize the weight of each ingredient in the controlled release formulation, a maximum plasma concentration, and an AUC provided in the composition, according to the guidance provided by Mehta et al. and Mulye, to ensure that the proper amount of drug is released at the designated time interval. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

The newly added claim limitation of the tablet formulation exhibiting the dissolution profile listed in claims 1, 19, and 21 is rendered obvious by the teachings of the prior art. Because the combination of the prior art renders the claimed controlled release formulation obvious, the dissolution profile would be a property of the formulation.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to combine the teachings of Mehta et al, which teach a composition for the improved dosing of methylphenidate, with Mulye and Beiman et al., which teach a controlled release pharmaceutical composition that comprises an enteric polymer that aids in delayed release of the drug. One having ordinary skill in the art would have been motivated to combine the teachings of Mehta et al. with Mulye and Beiman et al. to formulate a controlled release composition of methylphenidate to reduce abuse potential and for better patient compliance to treat nervous system disorders (as taught by Mehta et al.; Col. 1, lines 26-32).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is 571-272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Renee Claytor

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER